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Assessing reporting delays and the effective reproduction number: The Ebola epidemic in DRC, May 2018–January 2019

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ABSTRACT

On August 1, 2018, the Democratic Republic of Congo declared its 10th and largest outbreak of Ebola inflicting North Khivu and Ituri provinces. The spread of Ebola to Congolese urban centers along with deliberate attacks on the health care workers has hindered epidemiological surveillance activities, leading to substantial reporting delays. Reporting delays distort the epidemic incidence pattern misrepresenting estimates of epidemic potential and the outbreak trajectory. To assess the impact of reporting delays, we conducted a real-time analysis of the dynamics of the ongoing Ebola outbreak in the DRC using epidemiological data retrieved from the World Health Organization Situation Reports and Disease Outbreak News. We analyzed temporal trends in reporting delays, epidemic curves of crude and reporting-delay adjusted incidences and changes in the effective reproduction number, R_t. As of January 15, 2019, 663 Ebola cases have been reported in the Democratic Republic of Congo. The average reporting delay exhibited 81.1% decline from a mean of 17.4 weeks (95% CI 13–24.1) in May, 2018 to 3.3 weeks (95% CI 2.7–4.2) in September, 2018 (F-test statistic = 44.9, $p = 0.0067$). The Ebola epidemic has shown a two-wave pattern with the first surge in cases occurring between July 30 and August 13, 2018 and the second on September 24, 2018. During the last 4 generation intervals, the trend in the mean R_t has exhibited a slight decline (rho = -0.37, $p < 0.001$), fluctuating around 0.9 (range: 0–1.8). Our most recent estimate of R is at 0.9 (95% CI: 0.4, 1.1) during the last generation interval. Our most recent analysis of the Ebola outbreak in DRC indicates that the Ebola virus still active although transmission is characterized by a low fluctuating reproduction number. Yet, this pattern does not imply that the epidemic can be easily controlled particularly in the context of unstable epidemiological surveillance efforts hindered by unpredictable local violence.

1. Introduction

A total of 27 outbreaks of Ebola virus disease have been reported in Central Africa since the first Ebola outbreak in 1976. Among these, 10 of the outbreaks occurred in the Democratic Republic of Congo (DRC). While these outbreaks have been mostly limited to a small number of cases in rural communities (Coltart et al., 2017; Camacho et al., 2014; House, 2014; Althaus, 2015) an ongoing Ebola outbreak in DRC, reported on August 1, 2018 by the World Health Organization, is affecting urban areas of the provinces of North Khivu and Ituri in the northeast region that borders Uganda (Sun, 2018). Unfortunately, armed conflict in the Ebola-affected zone is hampering the outbreak response. In fact, deliberate attacks on the healthcare workers who are carrying out containment efforts have been reported (Petesch, 2018). This is the first and the largest Ebola outbreak reported in an active conflict zone that includes multiple armed military groups spread out in the Ebola-affected area (Alert, 2018; Claude et al., 2018).

As of January 15, 2019, the Ebola incidence curve of the outbreak in North Kivu, DRC, roughly displays a two-wave pattern (Fig. 2). The secondary surge in case incidence, starting on September 24, 2018, is likely associated with the effects of local armed conflict on control interventions (e.g., contact tracing, active case monitoring, vaccination campaigns) (Reijn et al., 2011; Anna, 2018). Fortunately, the Ebola outbreak does not appear to be following an increasing incidence growth pattern, but it appears to be following a steady incidence pattern with approximately ∼35 cases reported per week during the last two months of the epidemic. Ebola appears to be well established in the region with a total of 663 cases including 57 healthcare worker cases reported as of January 15, 2019 (WHO 2018, WHO 2019). Given the persistent moderate activity of the outbreak in North Khivu and Ituri,

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the Ebola virus is slowly spreading to new communities with potential expansion to neighboring provinces and countries (WHO 2018; WHO 2019).

Public awareness (e.g. media) and public health interventions (e.g. contact tracing) are often driven by reported outbreaks, subject to reporting delays. Substantial changes in reporting delays, e.g., the difference in the number of the days between the week of symptom onset and week of case reporting, may result from fluctuations in the effectiveness of control interventions taking place in an unpredictable conflict zone; therefore, it is even more important to monitor the temporal changes in reporting delays. Delays in reporting have the potential to distort the incidence curve of the epidemic, and in turn, estimates of transmission potential, forecasts of the outbreak trajectory, and the impact of control interventions (Reijn et al., 2011; Kelly-Hope, 2008). In the context of Ebola, factors influencing reporting delays include (i) difficulties in tracing and monitoring contacts for rapid case isolation, (ii) deliberate attacks on health care workers and suspension of health care outreach, (iii) resistance of sick individuals to seek medical care as soon as the symptoms start and (iv) population displacements (llunga, 2018; Shearer, 2018).

We are conducting a real-time analysis of the dynamics of the ongoing Ebola outbreak in DRC using epidemiological data retrieved from the WHO (World Health Organization) Situation Reports and Disease Outbreak News (WHO, 2018a; WHO 2019). For this purpose, we have analyzed and compared epidemic curves of crude and reporting-delay adjusted incidences from April 30, 2018 to January 15, 2019, and used adjusted incidence and statistical modeling to monitor changes in the effective reproduction number (R_t).

2. Data and methods

2.1. Ebola cases

Incidence data of the confirmed and probable cases of the ongoing Ebola outbreak in DRC (August 2018–January 2019) are publicly available from the WHO website (WHO 2018; WHO 2019). Data were manually extracted using WebPlotDigitizer (Rohatgi, 2018) from the weekly incidence curves published in Situation Reports and Disease Outbreak News Reports, which were published weekly, on variable week days (Table 1). The starting week of symptom onset was defined as April 30, 2018, based on the third Situation Report from WHO (WHO 2018) while the first date of reporting of cases was August 20, 2018 (WHO 2018). Dates of symptoms onset and reporting for each new Ebola case were retrieved by sequentially analyzing consecutive Ebola WHO reports (Yan, 2018). Because case reclassification has been conducted by WHO throughout the epidemic, we have reclassified non-cases on any specific reporting date by removing them from the dataset for a given reporting date. The most recent dataset (reporting date on 15-Jan-2019) is provided as a supplementary file.

2.2. Reporting delay adjusted incidence

It is important to note that the epidemic curves may be distorted not only by a reporting delay, but also by reporting patterns in different jurisdictions. Because the Ebola epidemic is still ongoing and the conditions in the field are volatile due to violent attacks in the region, it is vital to monitor reporting delays and adjust case incidence accordingly. For each case, reporting delay was calculated as the difference in the number of days between the date of reporting and the date of symptoms onset. The curve of crude incidence by date of symptoms onset was adjusted for the reporting delays using a nonparametric method that adapts survival analysis and life table techniques for use with right truncated data, described in previous works (Brookmeyer and Gail, 1994; Lawless, 1994; Yan and Chowell, 2019). This method works better when the numbers in data are moderately large, as large numbers give more precision, implying narrower confidence intervals. If the reporting delay itself is also long, then the estimated lower bounds tend to remain above the actual reported numbers. If data are sparse and meanwhile the underlying delay is not very long, then the confidence intervals tend to be larger. The corresponding R code to adjust incidence curves by reporting delays is available from the authors upon request. We also analyzed the monthly changes in reporting delays during the course of the epidemic with confidence intervals derived via bootstrapping with 500 replicates (Matlab Inc; Efron and Tibshirani, 1993). We employed linear regression (F-test, $\alpha = 0.05$) to assess temporal changes in reporting delays.

2.3. Effective reproduction number, R_t

Using the reporting-delay adjusted incidence curve, we estimated the effective reproduction number, R_t, defined as the average number of secondary cases generated per case at time t (for $t > 0$). R_t is a key indicator to monitor changes in transmission potential, as $R_t < 1$ indicates a decreasing trend in the epidemic whereas $R_t > 1$ indicates an upward trend in disease transmission. To estimate R_t we employed the renewal equation method previously described in refs. (Nishiura and Chowell, 2014; Nishiura and Chowell, 2009). The generation interval was assumed to follow a gamma distribution with a mean of 15.3 days and standard deviation (SD) of 9.1 days (Aylward et al., 2014). Specifically, based on the incidence at calendar time t_i denoted by I_i, and the discretized probability distribution of the generation interval denoted by ρ_i, the effective reproduction number can be estimated using the renewal equation (Fraser, 2007; Nishiura and Chowell, 2009):

$$R_{t_i} = \frac{I_i}{\sum_{j=0}^{i} I_{i-j}\rho_j}$$

where the denominator represents the total number of cases that contribute (as primary cases) to generating the number of new cases I_i (as secondary cases) at calendar time t_i. To derive uncertainty bounds around the curve of R_t, we estimated the R_t for 100 simulated curves generated through 100 realizations of the parametric bootstrapping method assuming a Poisson error structure (Chowell, 2017).

3. Results

As of January 15, 2019, 663 Ebola cases have been reported in the province of North Khivu and Ituri. The ongoing epidemic displays two epidemic waves, the first occurring between July 30 and August 13, 2018. The second case resurgence started on September 24, 2018 and approached a steady incidence pattern with an average of ~35 cases per week during the last two months of the epidemic. The average reporting delay exhibited a 81.1% decline from a mean of 17.4 weeks (95% CI: 13, 24.1) in May, 2018 to 3.3 weeks (95% CI: 2.7, 4.2) in September, 2018 (F-test, F-statistic = 44.9, $\alpha = 0.05$, $p = 0.0067$) (Fig. 1). The most recent estimate of the average reporting delay is 1.7 week (95% CI: 1.6, 1.9) for the last month of the epidemic (December 3, 2018–January 7, 2019).

Differences between the crude and the reporting-delay adjusted incidence curves are shown in Fig. 2. The largest difference can be observed in most recent part of the epidemic (December 31, 2018–January 14, 2019). Since the epidemic is still ongoing, data in recent weeks are subject to delays associated with data cleaning, case confirmation and reporting, and the unpredictable effects of the armed conflict on epidemiological surveillance efforts and public health interventions. Hence, it is important to emphasize that although reporting delays have decreased considerably, substantial fluctuations in reporting delays cannot be ruled out.

Fig. 3 displays the curve of the estimated effective reproduction number with 95% confidence intervals for four recent reporting dates: 13-November-2018, 2-December-2018, 16-December-2018, and 15-January-2019, using the reporting-delay adjusted incidence curve

Table 1
Ebola incidence cases according to the date of issuance and date of reporting from the WHO Situation Reports and Disease Outbreak News.

Situation report/disease outbreak news	Date of issue	Data of reporting	Total cases	incidence cases	Situation report/disease outbreak news citation
Situation Report 3	August 22, 2018	August 20, 2018	102	102	(WHO 2018)
Disease Outbreak News	August 24, 2018	August 22, 2018	103	1	(WHO 2018)
Situation Report 4	August 28, 2018	August 26, 2018	111	8	(WHO 2018)
Disease Outbreak News	August 31, 2018	August 29, 2018	115	4	(WHO 2018)
Situation Report 5	September 4, 2018	September 2, 2018	118	3	(WHO 2018)
Disease Outbreak News	September 7, 2018	September 5, 2018	127	9	(WHO 2018)
Situation Report 6	September 11, 2018	September 9, 2018	131	4	(WHO 2018)
Disease Outbreak News	September 14, 2018	September 12, 2018	137	6	(WHO 2018)
Situation Report 7	September 18, 2018	September 16, 2018	142	5	(WHO 2018)
Disease Outbreak News	September 20, 2018	September 18, 2018	142	0	(WHO 2018)
Situation Report 8	September 25, 2018	September 23, 2018	150	8	(WHO 2018)
Disease Outbreak News	September 27, 2018	September 25, 2018	147	0	(WHO 2018)
Situation Report 9	October 4, 2018	September 30, 2018,	161	14	(WHO 2018)
Disease Outbreak News	October 4, 2018	October 2, 2018	160	0	(WHO 2018)
Situation Report 10	October 9, 2018	October 7, 2018	160	0	(WHO 2018)
Disease Outbreak News	October 11, 2018	October 9, 2018	190	30	(WHO 2018)
Situation Report 11	October 17, 2018	October 15, 2018	210	20	(WHO 2018)
Disease Outbreak News	October 18, 2018	October 16, 2018	219	9	(WHO 2018)
Situation Report 12	October 23, 2018	October 21, 2018	238	19	(WHO 2018)
Disease Outbreak News	October 25, 2018	October 23, 2018	246	8	(WHO 2018)
Situation Report 13	October 30, 2018	October 28, 2018	272	26	(WHO 2018)
Disease Outbreak News	November 1, 2018	October 30, 2018	274	2	(WHO 2018)
Situation Report 14	November 6, 2018	November 4, 2018	294	20	(WHO 2018)
Disease Outbreak News	November 8, 2018	November 6, 2018	303	9	(WHO 2018)
Situation Report 15	November 13, 2018	November 11, 2018	333	30	(WHO 2018)
Disease Outbreak News	November 15, 2018	November 13, 2018	341	8	(WHO 2018)
Situation Report 16	November 21, 2018	November 18, 2018	370	29	(WHO 2018)
Disease Outbreak News	November 22, 2018	November 20, 2018	382	12	(WHO 2018)
Situation Report 17	November 28, 2018	November 25, 2018	419	37	(WHO 2018)
Disease Outbreak News	November 29, 2018	November 27, 2018	416	0	(WHO 2018)
Situation Report 18	December 5, 2018	December 2, 2018	444	28	(WHO 2018)
Disease Outbreak News	December 6, 2018	December 4, 2018	458	14	(WHO 2018)
Situation Report 19	December 12, 2018	December 10, 2018	495	37	(WHO 2018)
Disease Outbreak News	December 13, 2018	December 11, 2018	504	9	(WHO 2018)
Situation Report 20	December 18, 2018	December 16, 2018	537	33	(WHO 2018)
Disease Outbreak News	December 20, 2018	December 18, 2018	549	12	(WHO 2018)
Situation Report 21	December 27, 2018	December 25, 2018	585	36	(WHO 2018)
Disease Outbreak News	December 28, 2018	December 26, 2018	591	6	(WHO 2018)
Situation Report 22	January 3, 2019	January 1, 2019	608	17	(WHO 2019)
Disease Outbreak News	January 4, 2019	January 2, 2019	609	1	(WHO 2019)
Situation Report 23	January 8, 2019	January 6, 2019	625	16	(WHO 2019)
Disease Outbreak News	January 10, 2019	January 8, 2019	628	3	(WHO 2019)
Situation Report 24	January 16, 2019	January 14, 2019	657	29	(WHO 2019)
Disease Outbreak News	January 17, 2019	January 15, 2019	663	6	(WHO 2019)

according to symptoms onset. During the last 4 generation intervals, the trend in the daily mean R_t has exhibited a slight decline (rho = −0.37, $p < 0.001$), fluctuating around 0.9 (range: 0–1.8). Our most recent estimate of R is at 0.9 (95% CI: 0.4, 1.1) during the last generation interval of disease transmission.

4. Discussion

Our analysis shows that the reporting delays for the ongoing Ebola outbreak in DRC have declined substantially over the course of the epidemic (Swaan et al., 2018, WHO 2018; WHO 2019), but fluctuations

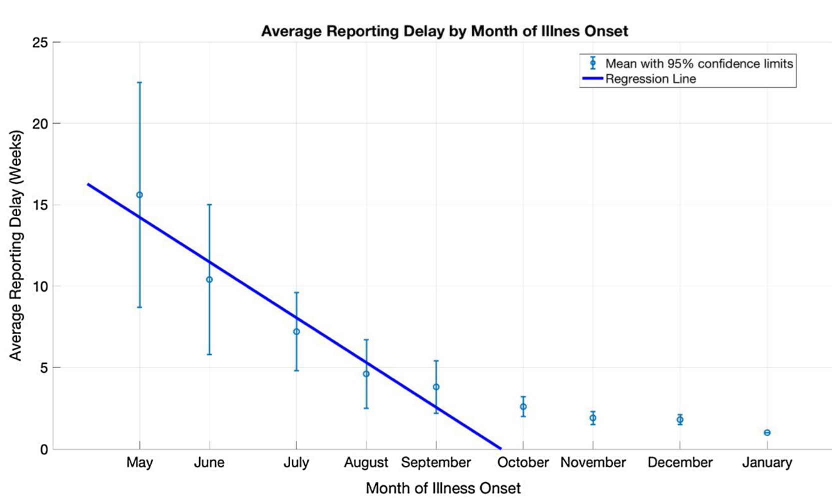

Fig. 1. Trend in the average reporting delay (in weeks) of the Ebola epidemic by month of illness onset from May 2018 to January 2019. Regression line fitted to the data for May to September, 2018 depicts temporal changes in the reporting delay. Trend declines significantly ($p = 0.0067$, $\alpha = 0.05$) with the progression of the epidemic till September, 2018. Error bars depict the confidence interval around mean reporting delay.

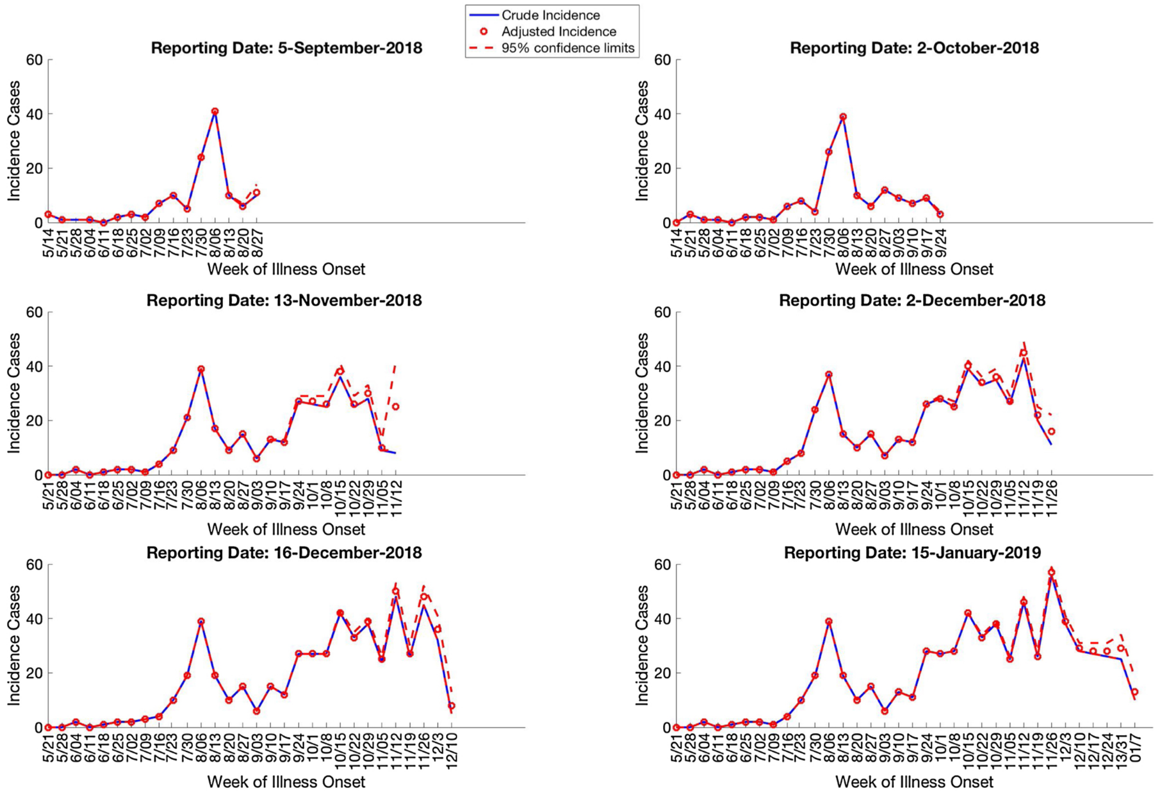

Fig. 2. Weekly Ebola incidence data from May 2018 to January 2019, unadjusted and reporting delay adjusted crude incidence by week of illness onset, at six reporting intervals: September 5, October 2, November 13, December 2, December 16, 2018 and January 15, 2019. Crude and adjusted incidences differ substantially for the most recent part of the epidemic. Crude incidence (Blue line), adjusted incidence (circles), 95% confidence interval around the adjusted incidence (dashed line) are presented in the figure.

in reporting delays cannot be ruled out owing to the unpredictable conditions brought about by the ongoing armed conflict in the Ebola-affected zone. Moreover, most recent estimates of the effective reproduction number indicate that the outbreak is active with a relatively steady incidence pattern. The large reporting delays during the early weeks of the outbreak (May-July, 2018) may be due to a healthcare worker strike as well as the effects of local insecurity in the region (Shearer, 2018; Frontières, 2018). Overall, the unpredictable effects of local armed conflict on control interventions have dramatically enhanced the complexity of this Ebola epidemic (Alert, 2018; Belluz, 2018).

A second wave of the epidemic was observed on September 24, 2018 and can be explained by the unpredictable violent attacks on health teams and community members in the Ebola affected areas, hampering epidemiological surveillance efforts (BBC, 2018; Soucheray, 2018). The Beni massacre in late September killed a large number of civilians, bringing outbreak response to a standstill for four days (Schnirring, 2018; Shearer, 2018; Belluz, 2018). Subsequently, red

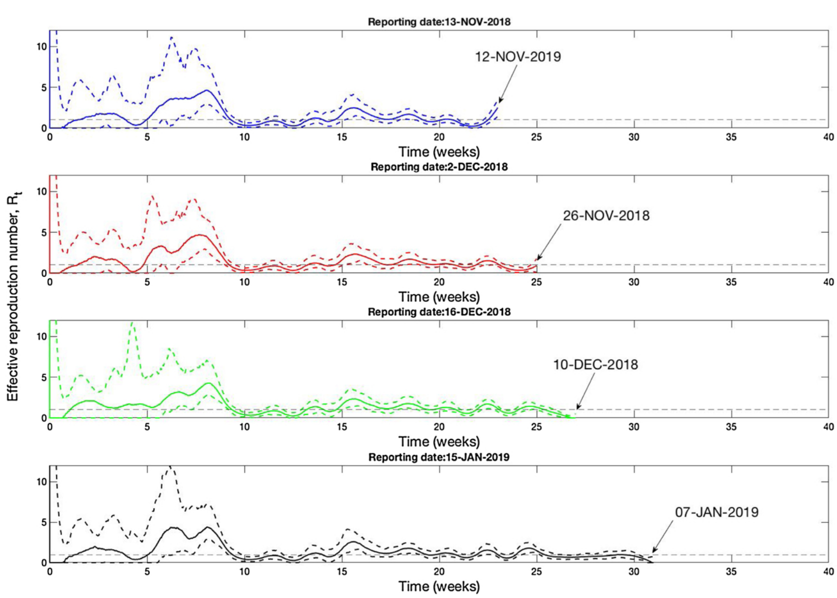

Fig. 3. Estimated effective reproduction number, R_t, for the Ebola epidemic derived utilizing reporting delay-adjusted incidence curve by week of onset of symptoms for four different reporting dates: November 13, 2018, December 2, 2018, December 16, 2018, and January 15, 2019. During the last 4 generation intervals, the trend in the daily mean R_t has exhibited a slight decline (rho = -0.37, $p < 0.001$), fluctuating around 0.9 (range: 0–1.8). Our most recent estimate of R is at 0.9 (95% CI: 0.4, 1.1) during the last generation interval of disease transmission. Horizontal dashed line indicates R_t at 1.0 threshold level.

cross volunteers have been targeted on multiple occasions in early October 2018, including an attack during a burial ritual and another attack on an ambulance (Anna, 2018; Reuters, 2018). These attacks on response teams have continued periodically through November 2018 to January 2019, followed by the retraction of US health response teams from the Ebola epicenter in North Khivu (Weber, 2018; Wilson, 2018; Schnirring, 2019a,b). Ebola cases among healthcare workers (about 8.6% of the total cases) have further complicated the Ebola response (Schnirring, 2018; Swetlitz, 2018).

Importantly, while recent reports indicate that Ebola virus is still active with a low reproduction number, this pattern does not imply that the epidemic can be easily controlled. The estimates of adjusted incidence also suggest uncertainty in the crude incidence reporting for the most recent month of the epidemic. Although, new cases are still being identified, the conflict situation and hampered outreach efforts could be affecting our ability to estimate the actual disease burden, with the most recent attack on health worker occurring on January 2, 2019 (Schnirring, 2019b). This suggests a likely potential for further case resurgences and longer reporting delays (Schnirring, 2019a,b), which could erroneously give the impression of a recent decline in case incidence when, in fact, the apparent decline is due to incomplete reporting of recent cases. This highlights the need to carefully monitor and interpret disease trends. Hence, the basic challenge lies in maintaining epidemiological surveillance systems in the context of an unstable environment disrupted by unpredictable violent attacks.

Conflict of interest

The authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.epidem.2019.01.003.

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